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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/718,316	11/20/2003	Ian Francis Hassan	4-30843D	9782
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1095	7590	06/25/2004
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NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 430/2
EAST HANOVER, NJ 07936-1080

EXAMINER

HUI, SAN MING R

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/718,316	Applicant(s) HASSAN ET AL.	
	Examiner San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/19/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a continuation of US 10/262,408, filed 10/01/2002, which is a continuation of US 09/942,805, filed 08/30/2001, which is a continuation of PCT/EP00/01722, filed 03/01/2000.

The preliminary amendments filed November 20, 2003 have been entered. Claims 1-20 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Briggner et al. (US Patent 5,874,063) in view of Gennaro et al. (Remington's Pharmaceutical Sciences, 1990, 18th edition, page 1699-1701, and 1706-1707), O'Connor (Pulmonary Pharmacology & Therapeutics, 1998;11:397-399), Sequeira et al. (US Patent 5,837,699), and Sequeira'393 (WO95/20393). Briggner et al., Gennaro et al., and Sequeira et al. are references of record in the parent application.

Briggner et al. teaches that inhalation drugs including β 2-agonist such as formoterol fumarate dihydrate, and steroids such as mometasone may be formulated into a mixture of the both agents in a finely divided dry particulates

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with a median diameter from 0.1 to 10 μm (See particularly claims 1, 7; also col. 2, line 1-6; col.5, example 6). Briggner et al. also teaches one pharmaceutical carrier useful for formulating the composition is lactose (See claim 9).

Briggner et al. does not expressly teach to use particularly mometasone to be employed in the inhalation formulation composition. Briggner et al. does not expressly teach that the composition would be in an aerosol forms and dispersed in halogen-substituted hydrocarbon propellant. Briggner et al. does not expressly teach the dosage and the weight ratio of formoterol fumarate dihydrate and mometasone to be 3 to 36 μg of formoterol and 25 to 800 μg of mometasone herein. Briggner et al. does not expressly teach the composition of formoterol fumarate dihydrate and mometasone could be separated into unit dosage forms in a pharmaceutical kit. Briggner et al. does not expressly teach the method of treating airway inflammatory disorder.

Gennaro et al. teaches that steroids could be formulated into aerosol, in which the steroids are dispersed in the propellant with a median diameter of 3 to 6 μm . (See particularly 1706, col. 2, third paragraph). Gennaro et al. also teaches the fluorinated hydrocarbon propellant 114 and propellant 114a are commonly used in aerosol dosage form (See page 1699, col. 2 second paragraph to page 1700, col. 2).

O'Connor teaches that employment of the combination of β -agonist and steroids in the management of asthma is more effective than that of either agent alone (See page 397, col. 2, last paragraph to page 398, col. 2, fourth paragraph). O'Connor also teaches that the addition of β -agonist, salmeterol, to

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fluticasone regimen resulting in a greater improvement in asthma control than increasing the dose of fluticasone alone (See page 398, col. 1, last paragraph). O'Connor also teaches that formoterol, combining with a steroid compound, budesonide, in low dose would produce an equal effect as the high dose budesonide (See page 398, col. 2, second paragraph).

Sequeira'393 discloses a method of treating respiratory inflammatory disorders such as asthma by administering a composition comprising the known steroidal anti-inflammatory agent, mometasone furoate in a pressurized oral inhaler to the patient (See, e.g., page 3, lines 16-19, page 10 lines 2-5). Moreover, it discloses that mometasone can be used as adjuvant therapy with bronchodilators in a therapeutic composition (See page 10, lines 5 and 9). Sequeira'393 also discloses the use of chlorofluorocarbon propellants broadly as well as the use of non-chlorofluorocarbon propellants with or without surfactants in the said inhaler (See page 10, lines 19-21).

Sequeira et al. teaches that the effective dosage range for mometasone would be 25 μ g to about 800 μ g for treating asthma (See particularly col. 4, line 21-47, claims 4 and 8).

It would have been obvious to one skill in the art when the invention was made to employ 25 to 800 μ g of mometasone and 3 to 36 μ g of formoterol into an aerosol dosage form, dispersed in fluorinated hydrocarbon propellant in a medicament composition and separate the composition into unit dosage forms in a pharmaceutical kit. It would have been obvious to one of ordinary skill in the art

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at the time the invention was made to employ the formoterol-mometasone composition in a method of treating asthma.

One of ordinary skill in the art would have motivated to employ 25 to 800 μ g of mometasone and 3 to 36 μ g of formoterol into an aerosol dosage form, dispersed in fluorinated hydrocarbon propellant in a medicament composition and separate the composition into unit dosage forms in a pharmaceutical kit because both 25 to 800 μ g of mometasone and 12 μ g of formoterol are known to be useful in treating asthma. Therefore, combining two agents which are known to be useful to treating asthma individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. Moreover, formoterol is known in use with a steroid in a method of treating asthma. It is also known that combining a long-acting, inhaled β 2-agonist with an inhaled glucocorticoid led to a greater improvement in the control of symptoms and in lung function than doubling the dose of the inhaled glucocorticoid. Therefore, combining any known steroids, including mometasone, with fomoterol would have been reasonably useful in a composition of treating asthma.

Furthermore, one of ordinary skill in the art would be reasonably expect to formulate formoterol-mometasone combination composition into a different inhaled dosage forms such as aerosol composition by dispersing the actives herein into a commonly used propellant, including fluorinated hydrocarbons. Reformulation of the known actives composition into a separate unit dosage form and place them into a pharmaceutical kit is within the purview of skilled artisan.

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In addition, one of ordinary skill in the art would have been motivated to employ the formoterol-mometasone composition in a method of treating asthma. As taught in O'Connor and Sequeira'393, formoterol, when combine with a steroid, is useful in treating asthma and mometasone is also known to be useful in treating asthma. Therefore, concomitantly administering both formoterol and mometasone, which is known as effective in treating asthma individually and in combination, together for treating asthma is *prima facie* obvious (*In re Kerkhoven* 205 USPQ 1069).

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the data presented in declaration of by Dr. Fromond filed April 5, 2002 in the parent application 09/942,805 have been considered and are found persuasive in regard to the presence of unexpected result of the combination of 1.5µg/kg of formoterol and 30µg/kg of mometasone. However, the evidence of unexpected results must be of a scope reasonably commensurate with the scope of the subject matter

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claimed. The claims herein are not limited to the synergistic amount of formoterol and mometasone.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


San-ming Hui
Patent Examiner
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